Survival of Titanium-Zirconium and Titanium Dental Implants in Cigarette-smokers and Never-smokers: A 5-Year Follow-up

Abdulaziz ALSAHHAF¹, Rana Saud ALSHAGROUD², Khulud Abdulrahman AL-AALI³, Raneem S. ALOFI⁴, Fahim VOHRA¹, Tariq ABDULJABBAR¹

Objective: To compare the peri-implant clinical and radiographic status around bone-level narrow-diameter titanium-zirconium (TiZr) implants and titanium (Ti) implants placed in cigarette-smokers (CS) and never-smokers (NS).

Methods: Partially edentulous CS and NS rehabilitated with TiZr and Ti implants were included. Demographic data and information regarding smoking habits were collected. Participants were divided into four groups: group-1, CS with TiZr implants; group-2, NS with TiZr implants; group-3, CS with Ti implants; and group-4, NS with Ti implants. 36, 30, 31 and 33 implants were placed in 24, 23, 24 and 25 male individuals in groups 1, 2, 3 and 4, respectively. Peri-implant plaque index (PI), bleeding on probing (BOP), probing depth (PD) and mesial and distal crestal bone loss (CBL) were measured. All patients were enrolled in biannual routine oral prophylaxis care at least until the fifth year of follow-up and oral hygiene instructions were reinforced at each recall appointment. P < 0.05 was considered statistically significant. **Results:** At the 3- and 5-year follow-ups, there was no statistically significant difference in the peri-implant PI, BOP, PD and CBL between individuals in all groups. In all groups, the implant success and survival rates were 100% and 100%, respectively, at the 5-year follow-up. **Conclusion:** The TiZr and Ti dental implants can remain clinically and radiographically stable in CS in a manner similar to NS. Routine oral hygiene maintenance plays an essential role in this regard.

Key words: *dental implant, crestal bone loss, peri-implant inflammation, cigarette smoking Chin J Dent Res* 2019;22(4):265–272; *doi:* 10.3290/j.cjdr.a43737

The stability of the peri-implant crestal bone levels plays an essential role in the long-term success and survival of dental implants¹⁻³. To minimise the risk of peri-implant crestal bone loss (CBL), modifications in the implant geometry and surface characteristics have

4 Department of Restorative Dental Sciences, College of Dentistry, King Saud University, Riyadh, Kingdom of Saudi Arabia.

Corresponding author: Dr Tariq ABDULJABBAR, Department of Prosthetic Dental Sciences, College of Dentistry, King Saud University, Riyadh 60169, Saudi Arabia. Tel: 966-014655444; Fax: 966-14678097. Email: tajabbar@ksu.edu.sa.

Chinese Journal of Dental Research

been proposed⁴⁻⁹. Titanium (Ti) is a biocompatible alloy¹⁰; however, studies^{11,12} have reported that the incorporation of zirconium in pure titanium alloy (in the proportion of 85% titanium and 15% zirconium) further improves the tensile and fatigue strength of the implant. Results from an experimental study in mini pigs showed that values for removal torque were significantly higher for the titanium-zirconium (TiZr) implants than for the Ti implants¹². In that study¹², the histologic results showed a significantly greater bone area within the chamber for the TiZr implants compared with the Ti implants. From a clinical perspective, 1-year followup results of a double-blind randomised controlled trial (RCT)¹³ showed that narrow-diameter bone-level TiZr dental implants exhibit the same outcomes (in terms of stability of crestal bone and success and survival rate) as conventional Ti bone-level implants. Similarly, a 36-month follow-up RCT by Quirynen et al¹⁴ showed

¹ Department of Prosthetic Dental Science, College of Dentistry, King Saud University, Riyadh, Kingdom of Saudi Arabia.

² Department of Oral Medicine and Diagnostic Science, King Saud University, Riyadh, Kingdom of Saudi Arabia.

³ Department of Clinical Dental Sciences, College of Dentistry, Princess Nourah Bint Abdulrahman University, Kingdom of Saudi Arabia.

no statistically significant difference in the soft tissue parameters and levels of crestal bone between the two groups. In that study¹⁴, the survival rate of TiZr and Ti alloy implants were 98.7% and 97.3%, respectively, at the 36-month follow-up. This suggests that TiZr and Ti demonstrate similar bone–tissue responses.

Habitual cigarette-smoking is a risk factor for periodontal and peri-implant soft tissue inflammation^{15,16} and loss of supporting alveolar bone around natural teeth and dental implants¹⁵⁻¹⁷. One explanation in this regard is that habitual smoking increases the formation and accumulation of advanced glycation endproducts (AGEs) in the periodontal tissues 18,19. Interactions between AGEs and their receptors (RAGE) induce the formation of matrix metalloproteinase (MMP)-1 and proinflammatory cytokines such as interleukin (IL)-6, by human gingival fibroblasts^{20,21}. Furthermore. nornicotine (a metabolite of nicotine) upregulates the expression of RAGE in the gingival tissues of smokers and stimulates the formation of reactive oxygen species, which jeopardise the periodontal tissues¹⁹. Besides compromising periodontal wound healing, these factors may also affect the healing of peri-implant tissues. To our knowledge, there are no studies in indexed literature that have compared the peri-implant soft tissue inflammatory parameters (plaque index [PI], bleeding on probing [BOP] and probing depth [PD]) and the CBL around narrow-diameter bone-level TiZr and Ti dental implants in cigarette-smokers (CS) and never-smokers (NS).

It is hypothesised that the peri-implant soft tissue inflammatory parameters (PI, BOP and PD) are worse and the CBL is higher around narrow-diameter bonelevel TiZr and Ti dental implants placed in CS compared with NS. The aim of the present 5-year follow-up retrospective study was to compare the peri-implant clinical and radiographic status around bone-level narrow-diameter TiZr dental implants and Ti implants placed in CS.

Materials and methods

The ethical approval was obtained from the ethics research committee of the Centre for Specialist Dental Practice and Clinical Research, Saudi Arabia. The present study was designed, conducted and reported following the Consolidation Standards of Reporting Trials (CONSORT) statement, and also following the guidelines recognised by the Declaration of Helsinki as revised in 2013 for experimentation involving human patients. A consent form was presented to all volunteering individuals. It was mandatory for all volunteering individuals to have read and signed the consent form before being included in the study. All participants were informed that they could withdraw their participation at any stage of the investigation with no consequences.

Inclusion and exclusion criteria

The inclusion criteria were:

- CS with TiZi implants;
- CS with Ti implants;
- NS with TiZi implants;
- NS with Ti implants.

The exclusion criteria were:

- Use of bone grafts or guided bone regeneration techniques during implant therapy;
- Individuals smoking multiple forms of smoking tobacco including cigarettes;
- Smokeless tobacco users;
- Alcohol users;
- Self-reported systemic diseases such as acquired immunodeficiency syndrome or human immunodeficiency virus infection, cardiovascular diseases, diabetes mellitus, hepatic disorders and/or renal disease.

Participants and grouping

Partially edentulous individuals rehabilitated with TiZr and Ti dental implants were included. Individuals who reported to have been smoking at least one cigarette daily for at least 12 months prior were defined as CS¹⁵; whereas individuals who reported to have never used any form of tobacco product were defined as NS^{22,23}. These individuals were recruited from the outpatient department of a local healthcare centre in Riyadh, Saudi Arabia. Clinical and radiographic examinations were performed at the Specialist Dental Center, Riyadh, Saudi Arabia. Participants were divided into four groups as follows: 24, 23, 24 and 25 male individuals were included in groups 1, 2, 3 and 4, respectively.

Questionnaire

Information regarding age, gender, duration and daily frequency of smoking, and family history of smoking was collected using a questionnaire. Information regarding daily tooth brushing and flossing was also gathered. The questionnaire was administered to all participants by a trained investigator.

Surgical procedure, implant-surface characteristics and prosthetic/loading protocols

All surgical and implant loading procedures were performed under local anaesthesia by a trained and experienced oral surgeon. Preoperatively, all patients received 1 g of amoxicillin as prophylactic antibiotic, starting the night before the surgery, and then 500 mg amoxicillin three times per day for a total of 7 days postoperatively. Patients with allergies were given clindamycin. In addition, pain medication (600 mg ibuprofen) was prescribed every 6 to 8 hours, as required. In all groups, participants were also advised to rinse with 0.2% chlorhexidine digluconate twice daily for 2 weeks starting on the first preoperative day. All TiZr implants (diameter 3.3 mm) (Roxolid, Institut Straumann, Basel, Switzerland) and Ti implants (diameter 4.1 mm) (Straumann Dental Implant System, Institut Straumann) were placed at bone level in the areas of missing maxillary and/or mandibular premolars and were left submerged for 3 to 4 months. All implants had moderately rough sandblasted and acid-etched (SLActive) surfaces. In summary, a midline crestal incision was made using a no. 15 surgical blade and mucoperiosteal flaps. The implant osteotomy sites were prepared according to a standard drilling sequence as described elsewhere²⁴. To minimise the risk of injury to the inferior alveolar nerve or the maxillary sinus, adjustable rubber stop devices were placed around the drills to locate them at least 1 mm shorter than the radiographic working length, above the mandibular canal or the maxillary sinus. All implants were placed in the centre of the healed alveolar ridge using an insertion torque of 30 to 35 Ncm. All implants were restored using cement-retained porcelain fused to metal fixed dental prostheses, which were delivered 8 to 10 weeks after the healing abutment connection.

Postoperative dental prophylaxis

All patients were enrolled in biannual routine oral prophylaxis care at least until the fifth year of followup, during which they underwent full-mouth mechanical plaque and calculus debridement using handheld ultrasonic scalers (VV DENTA, Guangxi, China). Oral hygiene instructions were reinforced at each recall appointment for individuals in both groups. Assessment of peri-implant clinical parameters and crestal bone loss

Two trained and calibrated examiners blinded to the participants group assessed the peri-implant soft tissue inflammatory parameters and the CBL. The overall kappa values for inter- and intra-examiner reliability were 0.86 and 0.88, respectively. The peri-implant PI^{25} . BOP and PD²⁵ were measured at six sites per implant (mesiobuccal, midbuccal, distobuccal, distolingual/palatal, midlingual/palatal and mesiolingual/palatal). The PD was measured to the nearest mm using a graded probe (Hu-Friedy Manufacturing, Chicago, IL, USA). Digital bitewing radiographs (Ektaspeed plus; Kodak, Rochester, NY, USA) were taken and viewed on a calibrated computer screen (Samsung SyncMaster digital TV monitor, Suwon City, Gyeonggi-do, Korea). The CBL was measured as the vertical distance from 2 mm below the implant-abutment interface to the most crestal part of the alveolar bone¹⁵. In each group, the mean mesial and distal peri-implant CBL was measured to the nearest mm using the software program Scion Image (Scion, Fredrick, MD, USA). The peri-implant mucositis was defined by the presence of soft tissue inflammation around the implant without any radiographic signs of CBL^{26,27}; and peri-implantitis was defined by the presence of soft tissue inflammation and CBL around the implant 26,27 .

Statistical analysis

The statistical analysis was performed using the software program SPSS (Version 18, Chicago, IL, USA). The peri-implant clinical (PI, BOP and PD) and radiographic (CBL) parameters were evaluated statistically for the CS and NS groups using the multiple comparisons test. Data including means and standard errors were compared. For multiple comparisons, the Bonferroni post-hoc test was performed. To determine the sample size in each group, a post hoc power analysis was performed using the software nQuery Advisor 6.0 (Statistical Solutions, Saugas, MA, USA), and to detect a 0.05 difference between the efficacy variables (PD and MBL) among CS and NS. It was estimated that inclusion of at least 23 individuals per group would vield a study power of 85%. P values less than 0.05 were considered statistically significant.

| - and 5-year follow-ups. | |
|------------------------------|--|
| ry parameters at the 3 | |
| and radiographic inflammatol | |
| Peri-implant clinical ar | |
| Table 1 | |

| Peri-implant | | 3-year fo | 3-year follow-up | | | 5-year fo | 5-year follow-up | |
|--|------------------------|------------------------|------------------------|------------------------|-------------------------|------------------------|------------------------|------------------------|
| parameters | Group-1 (mean ± SD) | Group-2 (mean ± SD) | Group-3 (mean ± SD) | Group-4 (mean ± SD) | Group-1 (mean ± SD) | Group-2 (mean ± SD) | Group-3 (mean ± SD) | Group-4 (mean ± SD) |
| Participants (n) | 24 | 23 | 24 | 25 | 24 | 23 | 24 | 25 |
| Number of implants placed (n) | 36 | 30 | 31 | 33 | 36 | 30 | 31 | 31 |
| Plaque index (%) | 27.3 ± 3.5 | 22.5 ± 1.8 | 26.4 ± 4.5 | 27.6 ± 2.8 | 24.3 ± 2.2 | 23.2 ± 2.1 | 22.6 ± 1.9 | 24.1 ± 1.6 |
| Bleeding on probing (%) | 6.4 ± 1.3 | 10.4 ± 0.8 | 5.5 ± 0.4 | 11.6 ± 0.7 | 8.3 ± 1.3 | 9.6 ± 1.4 | 5.8 ± 1.6 | 9.4 ± 2.1 |
| Probing depth (in mm) | 2.6 | 2.2 | 2.5 | 2.4 | 2.4 | 2.2 | 2.5 | 2.4 |
| Mean CBL (in mm) | 1.26 | 1.18 | 1.35 | 1.08 | 1.53 | 1.4 | 1.5 | 1.3 |
| Mesial CBL (in mm) | 1.2 | 1.1 | 1.3 | 1.1 | 1.5 | 1.4 | 1.5 | 1.3 |
| Distal CBL (in mm) | 1.3 | 1.2 | 1.4 | 1.0 | 1.6 | 1.4 | 1.5 | 1.3 |
| SD: standard deviation; CBL: crestal bone loss | loss | | | | | | | |

Results

General characteristics of the study groups ^{essen}

The mean age of individuals in groups 1, 2, 3 and 4 were 40.4 ± 5.1 , 45.6 ± 3.3 , 44.5 ± 3.1 and 43.7 ± 4.2 years, respectively. In groups 1 and 3, participants had a cigarette smoking history of 8.9 ± 2.6 and 10.3 ± 1.4 years, respectively. A family history of tobacco smoking was reported by 18, 4, 16 and 5 individuals in groups 1, 2, 3 and 4, respectively. Brushing teeth once every day was reported by 19, 20, 17 and 21 individuals in groups 1, 2, 3 and 4, respectively. None of the individuals in the groups reported to have ever used dental floss.

Clinical and radiographic parameters at the 3- and 5-year follow-ups

A total of 36, 30, 31 and 33 implants were placed in individuals in groups 1, 2, 3 and 4, respectively. At the 3- and 5-year follow-ups, there was no statistically significant difference in the peri-implant PI, BOP, PD and mesial and distal CBL between individuals in groups 1, 2, 3 and 4 (Table 1). There was no clinical evidence of peri-implant mucositis at the 3- and 5-year follow-ups. None of the radiographs showed evidence of peri-implantitis at the 3- and 5-year follow-ups, the implant success and survival rates were 100% and 100%, respectively, at the 5-year follow-up.

There was no statistically significant difference in PI, BOP, PD and mesial and distal CBL around implants placed in the maxilla and mandible among individuals in groups 1, 2, 3 and 4, at the 3-year follow-up (Figs 1 and 2) and at the 5-year follow-up (Figs 3 and 4).

Discussion

It was hypothesised that the peri-implant soft tissue inflammatory parameters (PI, BOP and PD) are worse and the CBL is higher around narrow-diameter bonelevel TiZr and Ti dental implants placed in CS compared with NS. This hypothesis was based on results from previous clinical studies^{15,22,23,25}, which showed significantly higher oral soft tissue inflammation and alveolar bone loss (ABL) around natural teeth and dental implants among CS compared with NS. In addition, previous in vitro studies^{18,19} have also reported that tobacco smoking is associated with increased interactions between AGEs and RAGE, which increase the production of destructive inflammatory cytokines such as interleukin 1 beta (IL-1 β) and IL-6 in body fluids. Raised levels of these destructive inflammatory cytokines in **Fig 1** Peri-implant plaque index (PI) (black bars) and bleeding on probing (BOP) (grey bars) in the maxilla and mandible among individuals in groups 1, 2, 3 and 4 at the 3-year followup. Data are presented as means ± 2 standard deviations.

Fig 2 Peri-implant probing depth (PD) (black bars) and crestal bone loss (CBL) (grey bars) in the maxilla and mandible among individuals in groups 1, 2, 3 and 4 at the 3-year followup. Data are presented as means ± 2 standard deviations.

Fig 3 Peri-implant plaque index (PI) (black bars) and bleeding on probing (BOP) (grey bars) in the maxilla and mandible among individuals in groups 1, 2, 3 and 4 at the 5-year followup. Data are presented as means ± 2 standard deviations.

Fig 4 Peri-implant probing depth (PD) (black bars) and crestal bone loss (CBL) (grey bars) in the maxilla and mandible among individuals in groups 1, 2, 3 and 4 at the 5-year followup. Data are presented as means ± 2 standard deviations.









269

the oral fluids have been associated with the aetiology of periodontal and peri-implant diseases²⁸⁻³⁰. An interesting finding of the present study was that there was no statistically significant difference in the peri-implant clinical (PI, BOP, PD) and radiographic (CBL) parameters around TiZr and Ti implants placed in CS and NS. It is important to interpret these results with caution as a number of factors may have influenced the reported results. Firstly, it is noteworthy that individuals in all the study groups were relatively young (approximately 40 years old). It is known that advancing age is a risk factor for ABL around natural teeth¹⁵. In the study by Javed et al¹⁵, the ABL around the teeth was significantly higher among individuals ≥ 60 years old compared with younger individuals (\leq 45 years old). It is therefore hypothesised that the CBL around TiZr and Ti dental implants is significantly higher among older individuals (≥ 60 years old) compared with relatively younger individuals (≤ 45 years old). Moreover, smokers with TiZr (group-1) and Ti (group-3) implants had a smoking history of approximately 9 and 10 years. It is likely that individuals with a longer history of smoking (for example 15 years or longer) exhibit worse peri-implant soft tissue inflammation and increased CBL compared with individuals with a shorter history of tobacco smoking, regardless of the type of implants (TiZr or conventional Ti) used. Further studies are needed to test these hypotheses.

It is noteworthy that in the present study, participants in all groups received bi-annual mechanical plaque and calculus debridement. Non-surgical periodontal therapy has been reported to play a role in minimising oral soft tissue inflammation $^{31-33}$. It is speculated that the biannual visits to oral healthcare providers may have encouraged the participants in all groups to routinely maintain their oral hygiene status. It is therefore likely that regular oral hygiene maintenance contributed towards maintaining healthy peri-implant soft tissue and minimising the CBL around TiZr and Ti implants among CS and NS. The present authors applaud the results of a previous study that reports that as long as the oral hygiene status is satisfactory, dental implants can exhibit a 100% survival rate³⁴. In our study, at least 70% of individuals in each group reported to brush their teeth once daily; and it has been reported that tooth brushing once daily is sufficient to maintain oral health and to prevent periodontal inflammation³⁵. However, Attin and Hornecker³⁵ emphasise that the general public should be educated that tooth brushing twice daily is the recommended domestic dental hygiene maintenance protocol; and oral healthcare providers (dentists and dental hygienists) should invest

Bone density and quality varies in the posterior maxilla and mandible mostly due to the presence of maxillary sinuses³⁶. In a 6-year follow-up clinical study³⁶, the CBL was significantly higher around implants placed in the posterior maxilla compared with the mandible. However, in the present study, no statistically significant difference in terms of clinical peri-implant parameters and CBL in the maxillae and mandibles among individuals in all groups was observed. Since all participants from our study received oral prophylaxis bi-annually, it is hypothesised that this factor may have contributed towards the maintenance of the periimplant soft and hard tissue status. In the present study, a family history of smoking was more often reported by individuals in groups 1 and 3 (CS) compared with individuals in groups 2 and 4 (NS). Indeed, smoking is a classic risk factor for soft tissue inflammation and alveolar bone loss around both natural teeth and dental implants^{15,37}. Although in our study there was no statistically significant difference in the CBL between CS and NS, it is imperative to elucidate to the public (particularly those who have family members who smoke) the detrimental effects of smoking on health, including dental and peri-implant tissue health.

A limitation of the present study was that individuals with systemic diseases were not included. It is well known that poorly controlled diabetes mellitus is a significant risk factor for peri-implant diseases (periimplant mucositis and peri-implantitis)³⁸. In addition, smokeless tobacco users were not included in the study. It is therefore likely that the CBL around short implants is significantly higher among CS with poorly controlled diabetes and CS chewing smokeless tobacco products compared with systemically healthy CS and CS not using other forms of tobacco products, respectively. Furthermore, all participants in our investigation were male. There is a possibility that irrespective of smoking, hormonal changes in females (particularly in the postmenopausal phase) may affect the oral soft and hard tissue status around short implants compared with males. Further studies are needed to clarify these questions.

Conclusion

TiZr and Ti dental implants can remain clinically and radiographically stable in CS in a manner similar to NS. Routine oral hygiene maintenance plays an essential role in this regard.

Acknowledgments

The authors extend their appreciation to the Deanship of Scientific Research at King Saud University, Riyadh, Saudi Arabia for funding this work.

Conflicts of interest

The authors declare no conflicts of interest related to this study.

Author contribution

Drs Tariq ABDULJABBAR, Fahim VOHRA, Rana Saud ALSHAGROUD, and Khulud Abdulrahman AL-AALI drafted the manuscript; Dr Khulud Abdulrahman AL-AALI performed the statistical analysis; Drs Tariq ABDULJABBAR and Fahim VOHRA supervised the study. All the authors were involved in the conception and design of the study, in the acquisition, analysis and interpretation of data and critical revision of the manuscript. Also, all the authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis, and approved the final submitted version.

(Received Feb 2, 2019; accepted April 11, 2019)

References

- Al Amri MD, Abduljabbar TS, Al-Johany SS, Al Rifaiy MQ, Alfarraj Aldosari AM, Al-Kheraif AA. Comparison of clinical and radiographic parameters around short (6 to 8 mm in length) and long (11 mm in length) dental implants placed in patients with and without type 2 diabetes mellitus: 3-year follow-up results. Clin Oral Implants Res 2017;28:1182–1187.
- Al Amri MD, Kellesarian SV, Al-Kheraif AA, Malmstrom H, Javed F, Romanos GE. Effect of oral hygiene maintenance on HbA1c levels and peri-implant parameters around immediately-loaded dental implants placed in type-2 diabetic patients: 2 years follow-up. Clin Oral Implants Res 2016;27:1439–1443.
- Becker J, Ferrari D, Mihatovic I, Sahm N, Schaer A, Schwarz F. Stability of crestal bone level at platform-switched non-submerged titanium implants: a histomorphometrical study in dogs. J Clin Periodontol 2009;36:532–539.
- Calvo-Guirado JL, López-López PJ, Pérez-Albacete Martínez C, et al. Peri-implant bone loss clinical and radiographic evaluation around rough neck and microthread implants: a 5-year study. Clin Oral Implants Res 2018;29:635–643.
- Romanos GE, Javed F. Platform switching minimises crestal bone loss around dental implants: truth or myth? J Oral Rehabil 2014;41:700– 708.
- Ghanem A, Kellesarian SV, Abduljabbar T, Al-Hamoudi N, Vohra F, Javed F. Role of osteogenic coatings on implant surfaces in promoting bone-to-implant contact in experimental osteoporosis: a systematic review and meta-analysis. Implant Dent 2017;26:770–777.

- Javed F, Al Amri MD, Kellesarian SV, Al-Askar M, Al-Kheraif AA, Romanos GE. Laminin coatings on implant surfaces promote osseointegration: fact or fiction? Arch Oral Biol 2016;68:153–161.
- Javed F, Vohra F, Zafar S, Almas K. Significance of osteogenic surface coatings on implants to enhance osseointegration under osteoporotic-like conditions. Implant Dent 2014;23:679–686.
- Kellesarian SV, Subhi ALHarthi S, Saleh Binshabaib M, Javed F. Effect of local zoledronate delivery on osseointegration: a systematic review of preclinical studies. Acta Odontol Scand 2017;75: 530–541.
- Ferraris S, Vitale A, Bertone E, Guastella SA, Cassinelli C, Pan J, Spriano S. Multifunctional commercially pure titanium for the improvement of bone integration: multiscale topography, wettability, corrosion resistance and biological functionalization. Mater Sci Eng C Mater Biol Appl 2016;60:384–393.
- Kobayashi E, Matsumoto S, Doi H, Yoneyama T, Hamanaka H. Mechanical properties of the binary titanium-zirconium alloys and their potential for biomedical materials. J Biomed Mater Res 1995;29:943–950.
- Gottlow J, Dard M, Kjellson F, Obrecht M, Sennerby L. Evaluation of a new titanium-zirconium dental implant: a biomechanical and histological comparative study in the mini pig. Clin Implant Dent Relat Res 2012;14:538–545.
- Al-Nawas B, Brägger U, Meijer HJ, et al. A double-blind randomized controlled trial (RCT) of Titanium-13Zirconium versus Titanium Grade IV small-diameter bone level implants in edentulous mandibles – results from a 1-year observation period. Clin Implant Dent Relat Res 2012;14:896–904.
- 14. Quirynen M, Al-Nawas B, Meijer HJ, et al. Small-diameter titanium Grade IV and titanium-zirconium implants in edentulous mandibles: three-year results from a double-blind, randomized controlled trial. Clin Oral Implants Res 2015;26:831–840.
- Javed F, Näsström K, Benchimol D, Altamash M, Klinge B, Engström PE. Comparison of periodontal and socioeconomic status between subjects with type 2 diabetes mellitus and non-diabetic controls. J Periodontol 2007;78:2112–2119.
- Rinke S, Ohl S, Ziebolz D, Lange K, Eickholz P. Prevalence of periimplant disease in partially edentulous patients: a practice-based cross-sectional study. Clin Oral Implants Res 2011;22:826–833.
- 17. Veitz-Keenan A. Marginal bone loss and dental implant failure may be increased in smokers. Evid Based Dent 2016;17:6–7.
- Katz J, Yoon TY, Mao S, Lamont RJ, Caudle RM. Expression of the receptor of advanced glycation end products in the gingival tissue of smokers with generalized periodontal disease and after nornicotine induction in primary gingival epithelial cells. J Periodontol 2007;78:736–741.
- Katz J, Caudle RM, Bhattacharyya I, Stewart CM, Cohen DM. Receptor for advanced glycation end product (RAGE) upregulation in human gingival fibroblasts incubated with nornicotine. J Periodontol 2005;76:1171–1174.
- Yu S, Li H, Ma Y, Fu Y. Matrix metalloproteinase-1 of gingival fibroblasts influenced by advanced glycation end products (AGEs) and their association with receptor for AGEs and nuclear factor-κB in gingival connective tissue. J Periodontol 2012;83:119–126.
- Wendell KJ, Stein SH. Regulation of cytokine production in human gingival fibroblasts following treatment with nicotine and lipopolysaccharide. J Periodontol 2001;72:1038–1044.
- Javed F, Abduljabbar T, Vohra F, Malmstrom H, Rahman I, Romanos GE. Comparison of periodontal parameters and self-perceived oral symptoms among cigarette smokers, individuals vaping electronic cigarettes, and never-smokers. J Periodontol 2017;88:1059– 1065.
- Javed F, Al-Kheraif AA, Al Amri MD, et al. Periodontal status and whole salivary cytokine profile among smokers and never-smokers with and without prediabetes. J Periodontol 2015;86:890–898.



- 24. Giro G, Tovar N, Marin C, et al. The effect of simplifying dental implant drilling sequence on osseointegration: an experimental study in dogs. Int J Biomater 2013;2013:230310.
- 25. Javed F, Al-Kheraif AA, Rahman I, et al. Comparison of clinical and radiographic periodontal status between habitual water-pipe smokers and cigarette smokers. J Periodontol 2016;87:142–147.
- 26. Lang NP, Berglundh T; Working Group 4 of Seventh European Workshop on Periodontology. Periimplant diseases: where are we now? – consensus of the Seventh European Workshop on Periodontology. J Clin Periodontol 2011;38 Suppl 11:178–181.
- Zitzmann NU, Berglundh T. Definition and prevalence of periimplant diseases. J Clin Periodontol 2008;35:286–291.
- Akram Z, Abduljabbar T, Abu Hassan MI, Javed F, Vohra F. Cytokine profile in chronic periodontitis patients with and without obesity: a systematic review and meta-analysis. Dis Markers 2016;2016:4801418.
- Javed F, Ahmed HB, Mikami T, Almas K, Romanos GE, Al-Hezaimi K. Cytokine profile in the gingival crevicular fluid of rheumatoid arthritis patients with chronic periodontitis. J Investig Clin Dent 2014;5:1–8.
- Javed F, Al-Hezaimi K, Salameh Z, Almas K, Romanos GE. Proinflammatory cytokines in the crevicular fluid of patients with periimplantitis. Cytokine 2011;53:8–12.
- Corbella S, Francetti L, Taschieri S, De Siena F, Fabbro MD. Effect of periodontal treatment on glycemic control of patients with diabetes: a systematic review and meta-analysis. J Diabetes Investig 2013;4:502–509.

- 32. Javed F, Ahmed HB, Mehmood A, Bain C, Romanos GE. Effect of nonsurgical periodontal therapy (with or without oral doxycycline delivery) on glycemic status and clinical periodontal parameters in patients with prediabetes: a short-term longitudinal randomized casecontrol study. Clin Oral Investig 2014;18:1963–1968.
- 33. Javed F, Kellesarian SV, Al-Kheraif AA, et al. Effect of Nd:YAG laser-assisted non-surgical periodontal therapy on clinical periodontal and serum biomarkers in patients with and without coronary artery disease: a short-term pilot study. Lasers Surg Med 2016;48:929–935.
- Degidi M, Nardi D, Piattelli A. 10-year follow-up of immediately loaded implants with TiUnite porous anodized surface. Clin Implant Dent Relat Res 2012;14:828–838.
- 35. Attin T, Hornecker E. Tooth brushing and oral health: how frequently and when should tooth brushing be performed? Oral Health Prev Dent 2005;3:135–140.
- 36. Ozgur GO, Kazancioglu HO, Demirtas N, Deger S, Ak G. Risk factors associated with implant marginal bone loss: a retrospective 6-year follow-up study. Implant Dent 2016;25:122–127.
- 37. ALHarthi SS, BinShabaib MS, Ahmed HB, Mehmood A, Khan J, Javed F. Comparison of peri-implant clinical and radiographic inflammatory parameters among cigarette and waterpipe (narghile) smokers and never-smokers. J Periodontol 2018;89:213–218.
- Javed F, Romanos GE. Impact of diabetes mellitus and glycemic control on the osseointegration of dental implants: a systematic literature review. J Periodontol 2009;80:1719–1730.